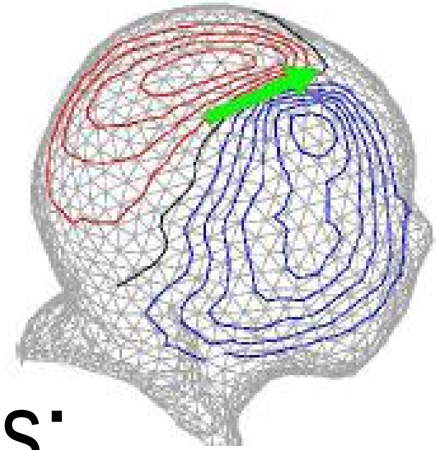


MEG in Clinical Pediatrics: Developmental Considerations and Effect of Early Brain Lesions

Päivi Nevalainen, MD PhD

Dept of Clinical Neurophysiology, Children's hospital and BioMag laboratory, HUS medical imaging center

Helsinki University Hospital and University of Helsinki, Finland

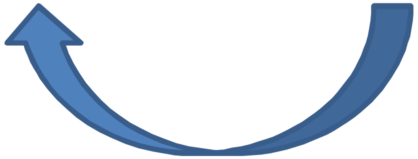
Clinical paediatric MEG

Individual level

- Epilepsy
- Functional mapping

Group level (disease mechanisms)

- Brain injury
  - Preterm birth
  - Perinatal stroke & other perinatal compromize
  - CP

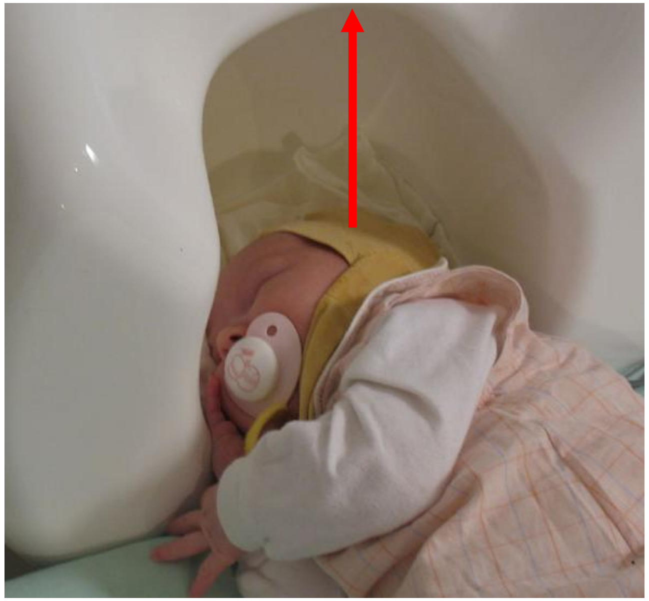


Neurophysiological biomarkers for
diagnostics,
outcome prediction,
individualized treatment?

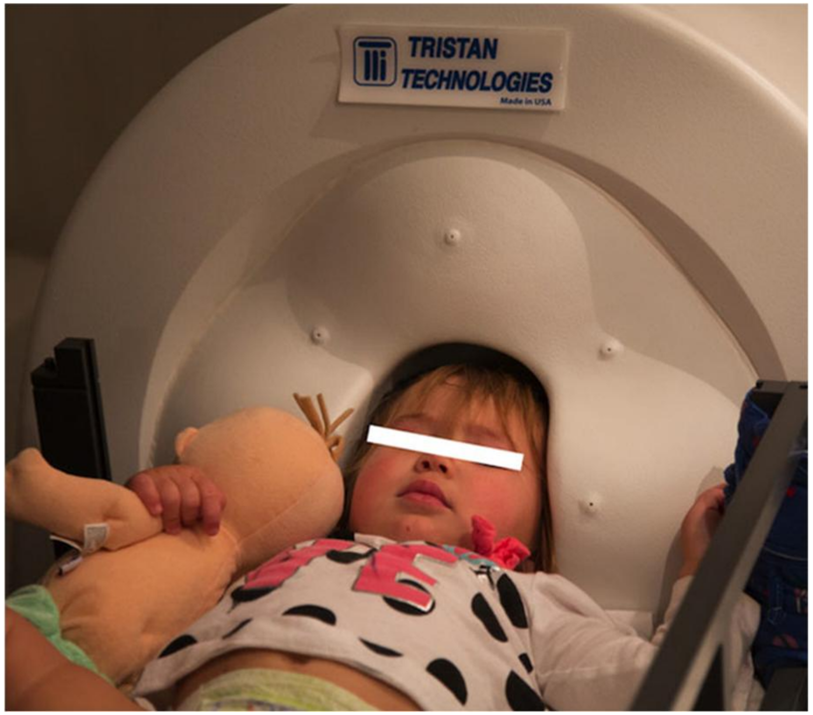
Challenges of pediatric MEG

- Co-operation and staying still
  - Neonates recorded during sleep
  - Head movement compensation

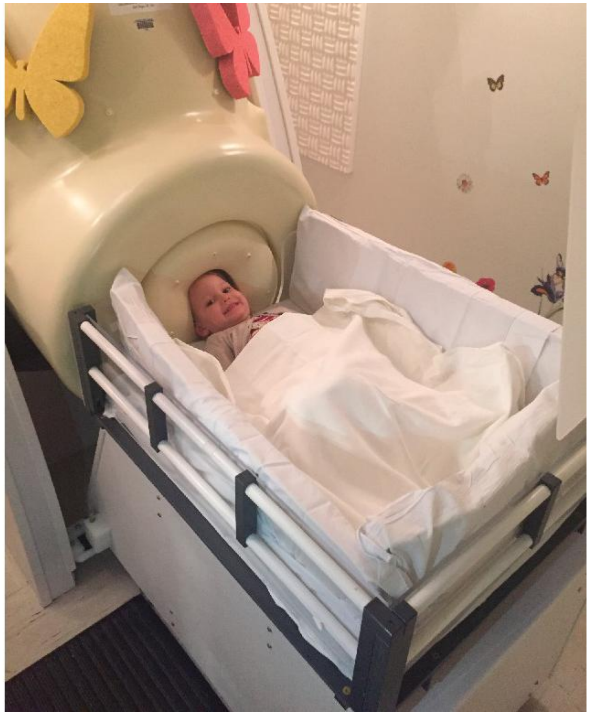
- Helmet size



Pediatric devices



*“Artemis 123” From: Roberts et al.,
Front Hum Neurosci. 2014; 8: 99.*



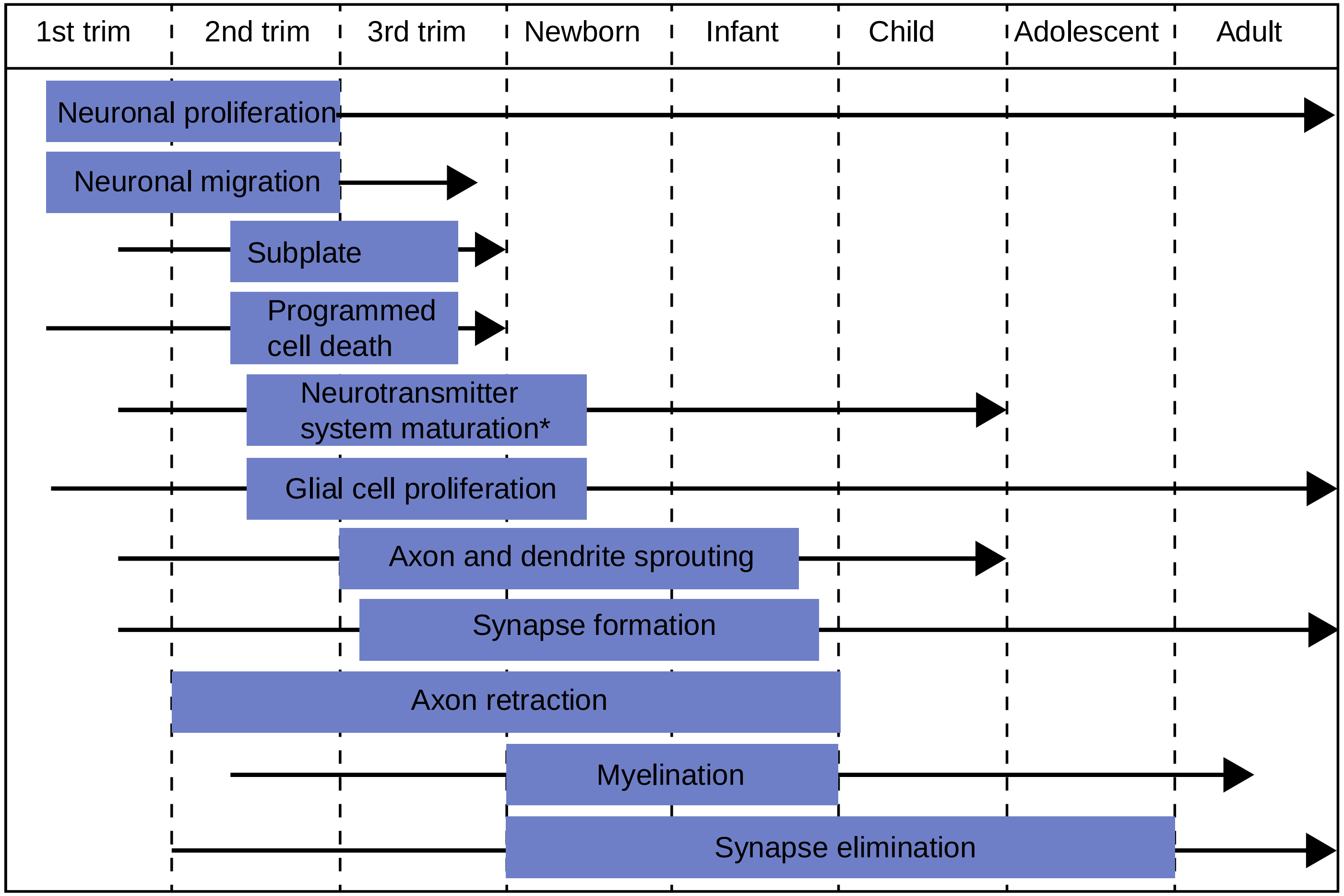
*“BabyMEG” From Okada et al., Review
of Scientific Instruments, 2016*

Advantages of MEG in pediatric studies

- Noninvasive and painless
- Excellent temporal resolution
- Good spatial resolution
  - Less sensitive to changes in tissue properties during development (or effects of large lesions) than EEG
  - Well-suited to study developmental phenomena over different age groups and patients with brain lesions

Brain development

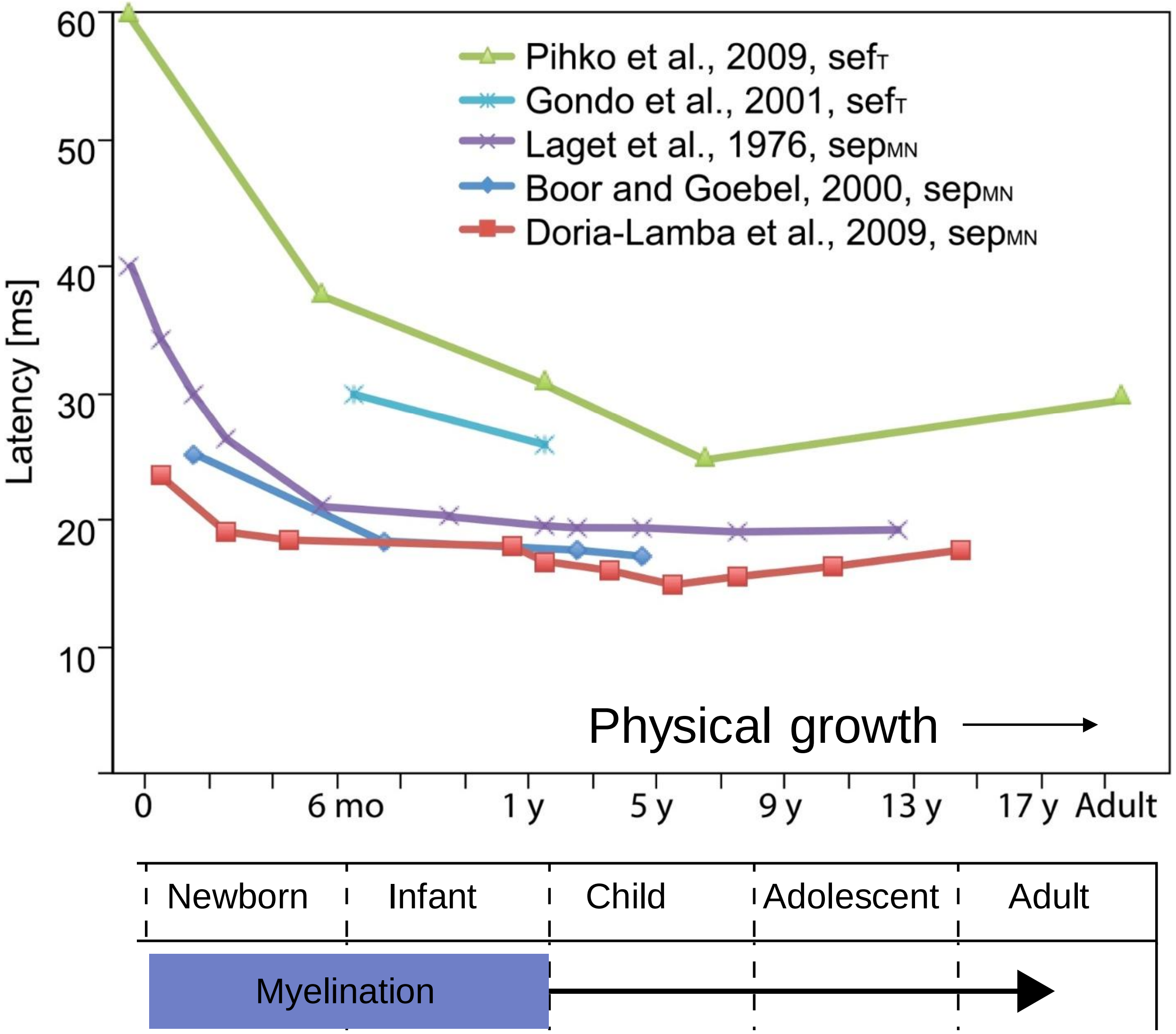
- Genetically regulated
- Refined by experience
- Role of neural activity!!



1st trim
2nd trim
3rd trim
Newborn
Infant
Child
Adolescent
Adult

Neuronal proliferation
Neuronal migration
Subplate
Programmed cell death
Neurotransmitter system maturation*
Glial cell proliferation
Axon and dendrite sprouting
Synapse formation
Axon retraction
Myelination
Synapse elimination

Somatosensory evoked responses



Major differences in activation pattern of primary somatosensory cortex

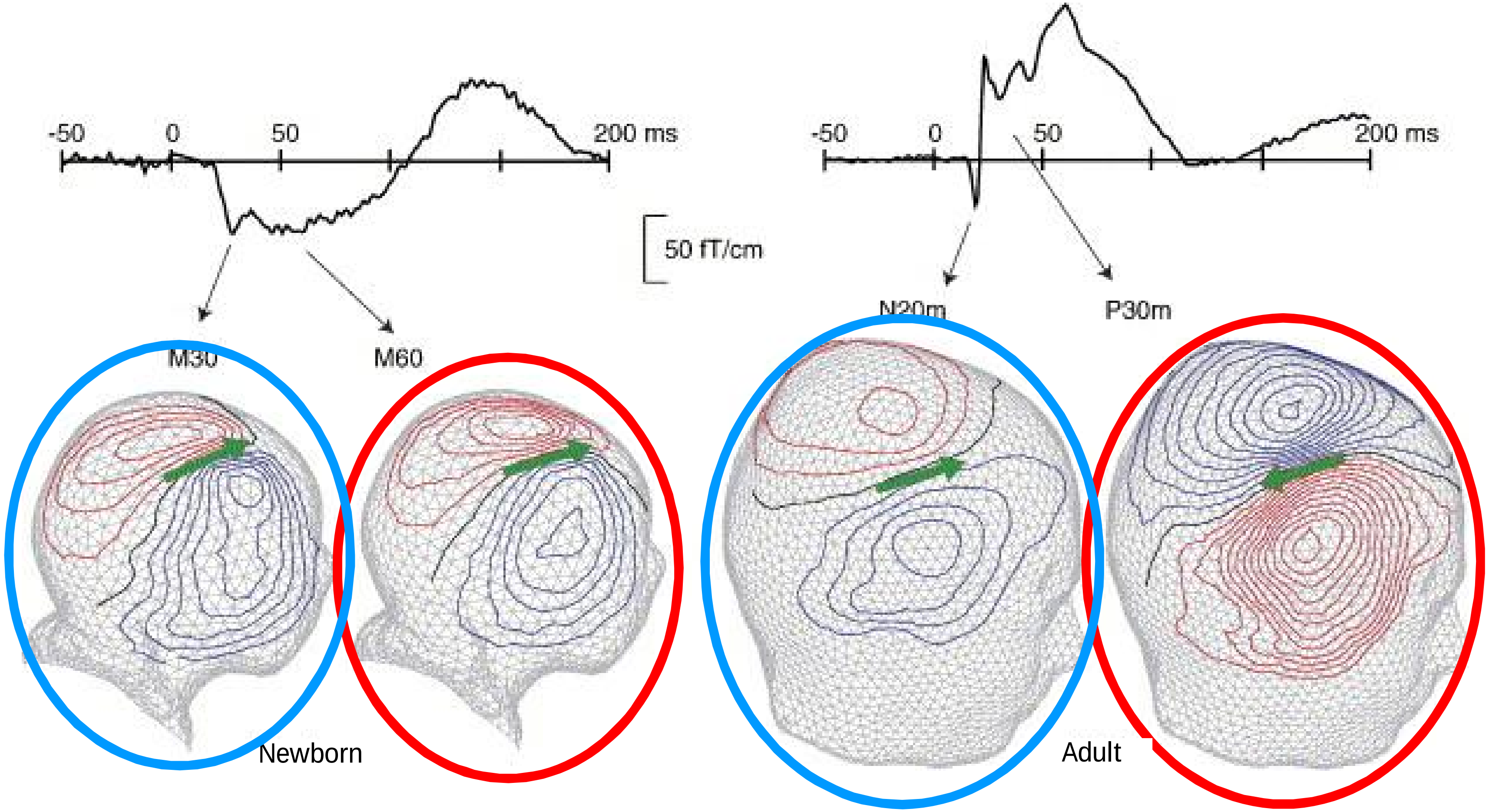


Figure from Lauronen et al., 2006

Movement related fields show opposite source orientation in 4-y-olds and adults

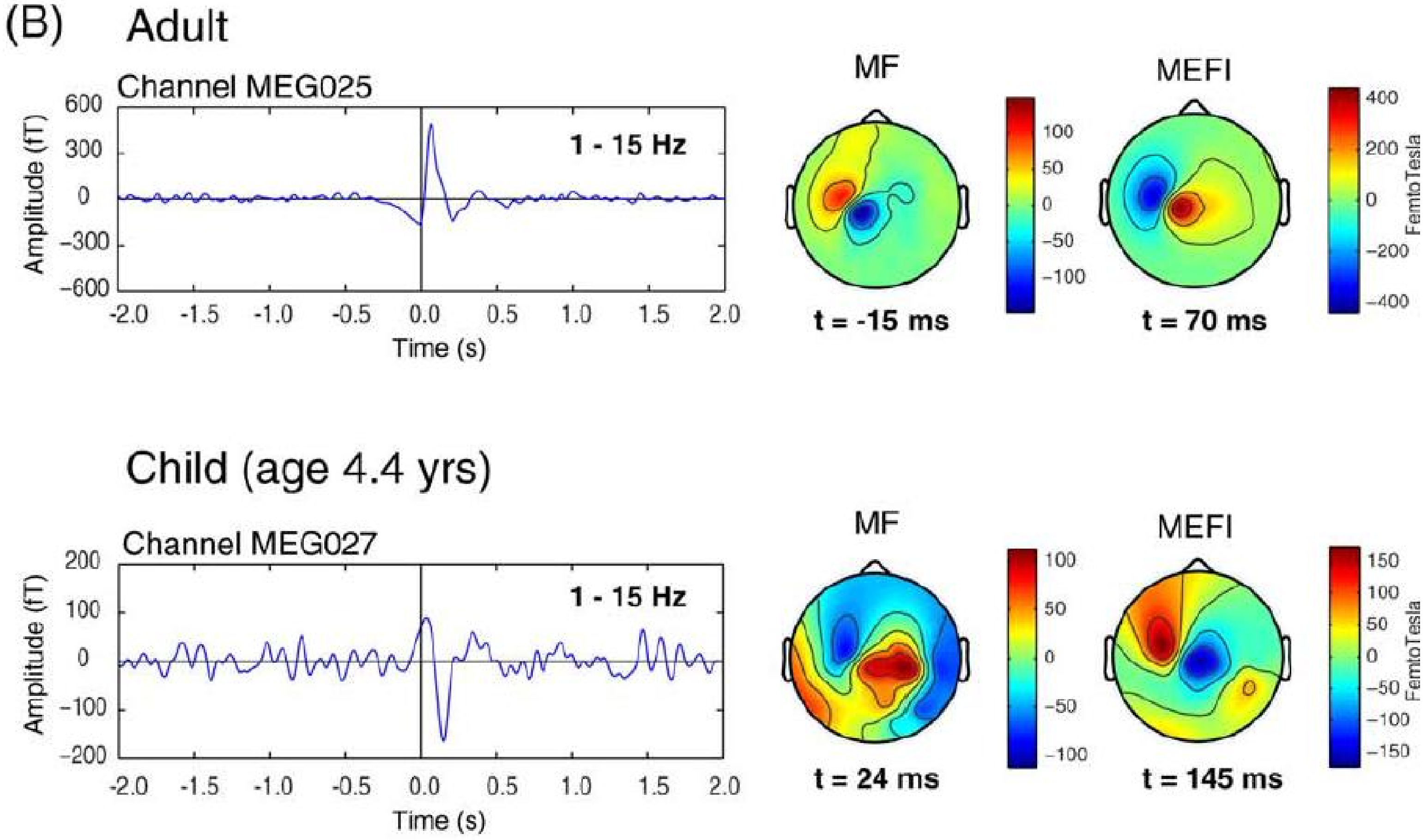


Figure from Cheyne et al., 2014

Systematic development of SEFs with age

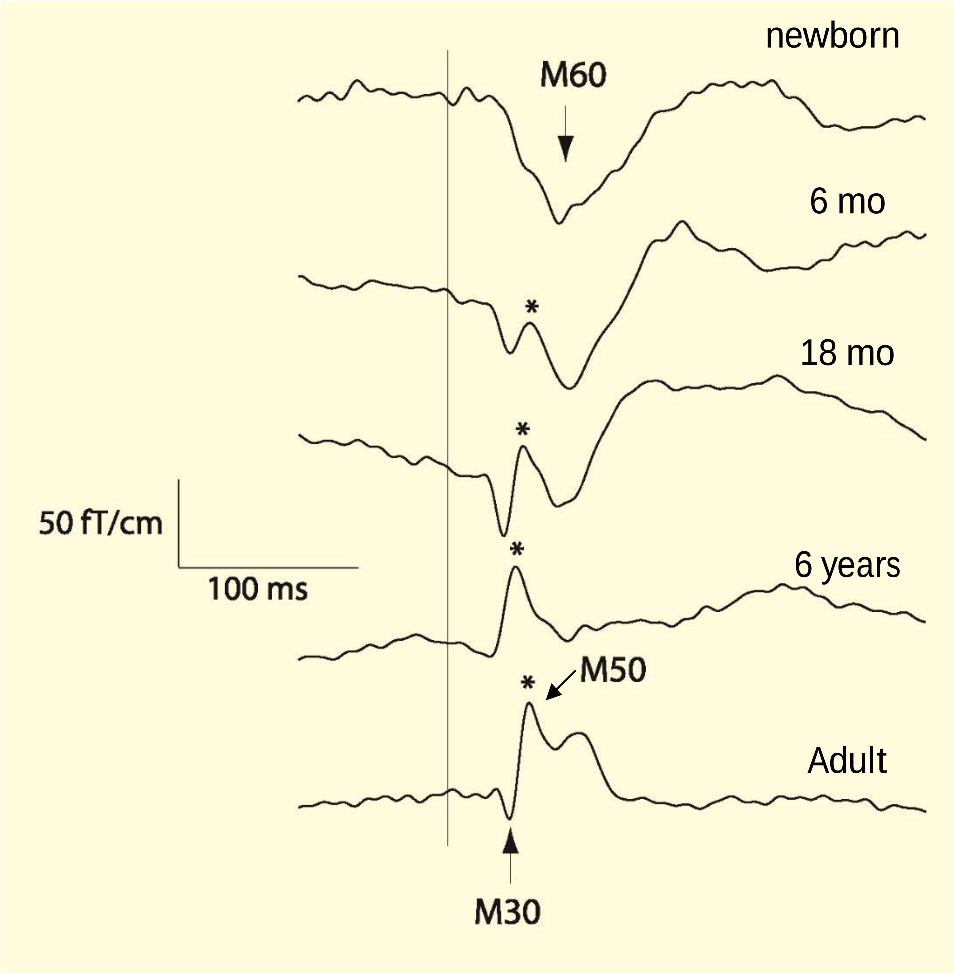


Figure from Pihko et al., 2009

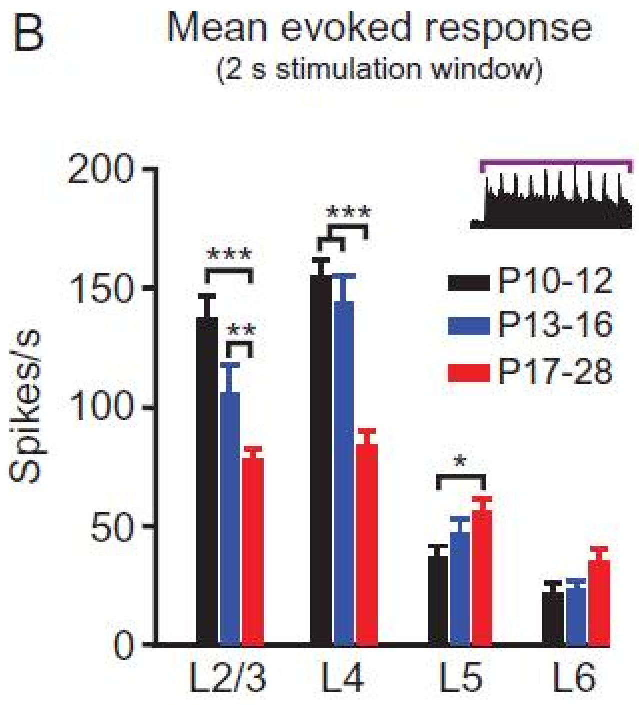
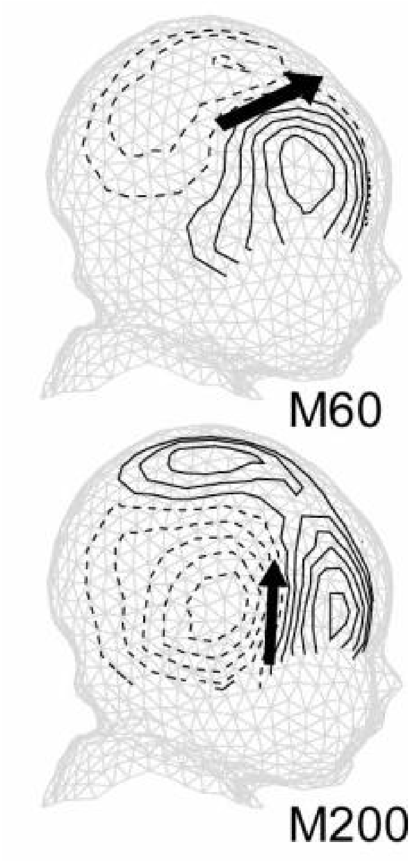
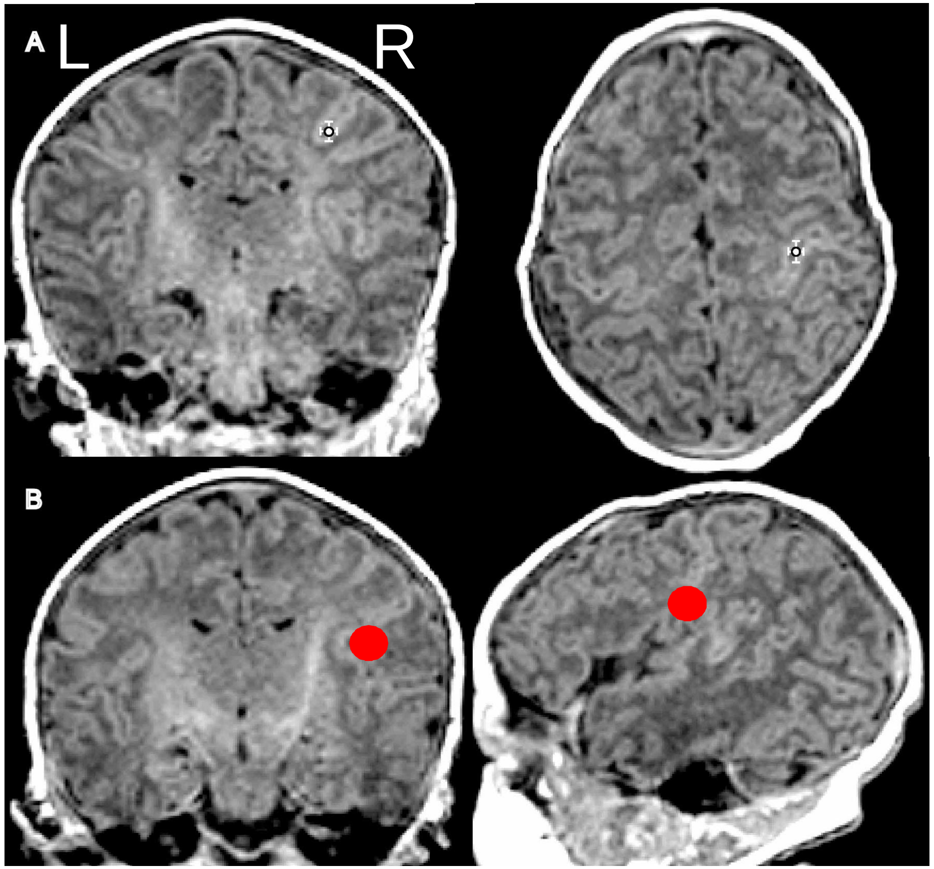


Figure from van der Bourg et al., 2016

Secondary somatosensory areas are activated in quiet sleep

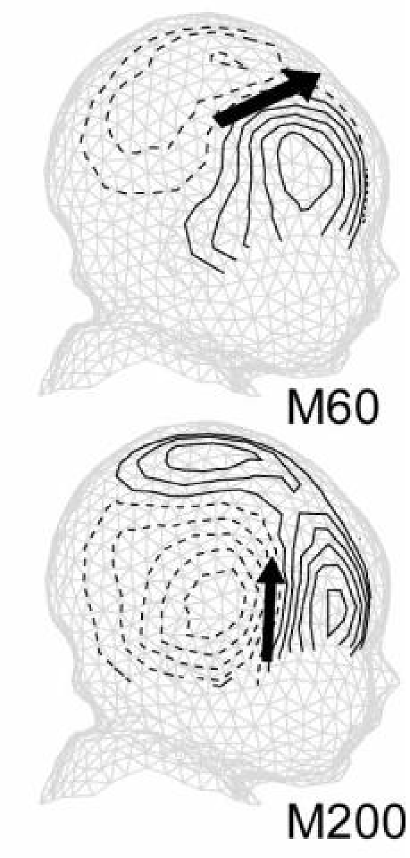
Newborns still build their cortical networks during sleep?





Nevalainen et al., 2008; 2015; Rahkonen et al., 2013

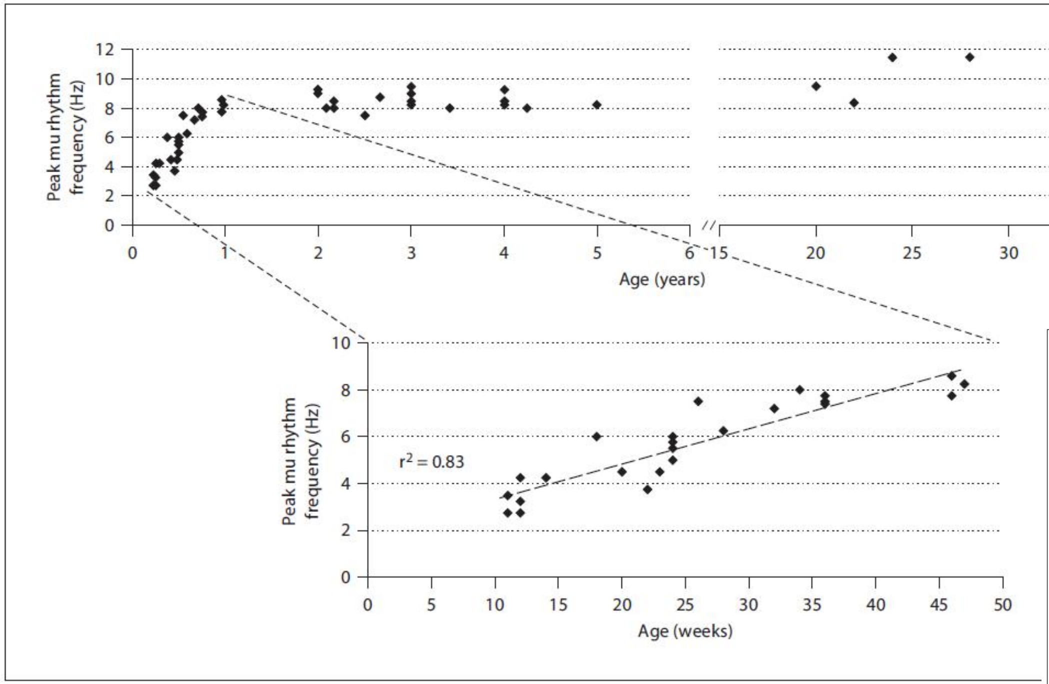
Secondary somatosensory areas are activated in quiet sleep

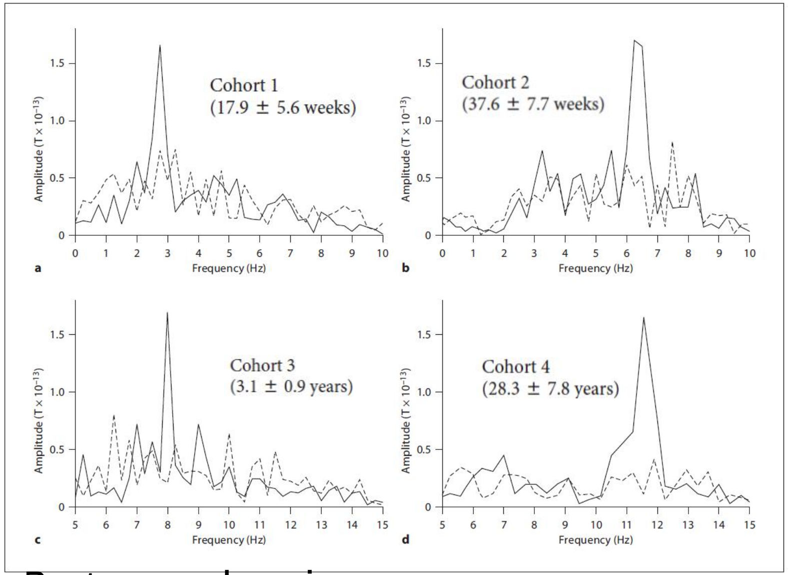


Preterm infants with SII responses missing ➔ worse neuromotor outcome at age 2 years

Nevalainen et al., 2008; 2015; Rahkonen et al., 2013

Development of sensorimotor oscillations





Rest vs. prehension

Figure from Berchicci et al., 2011

Movement related changes in beta oscillations

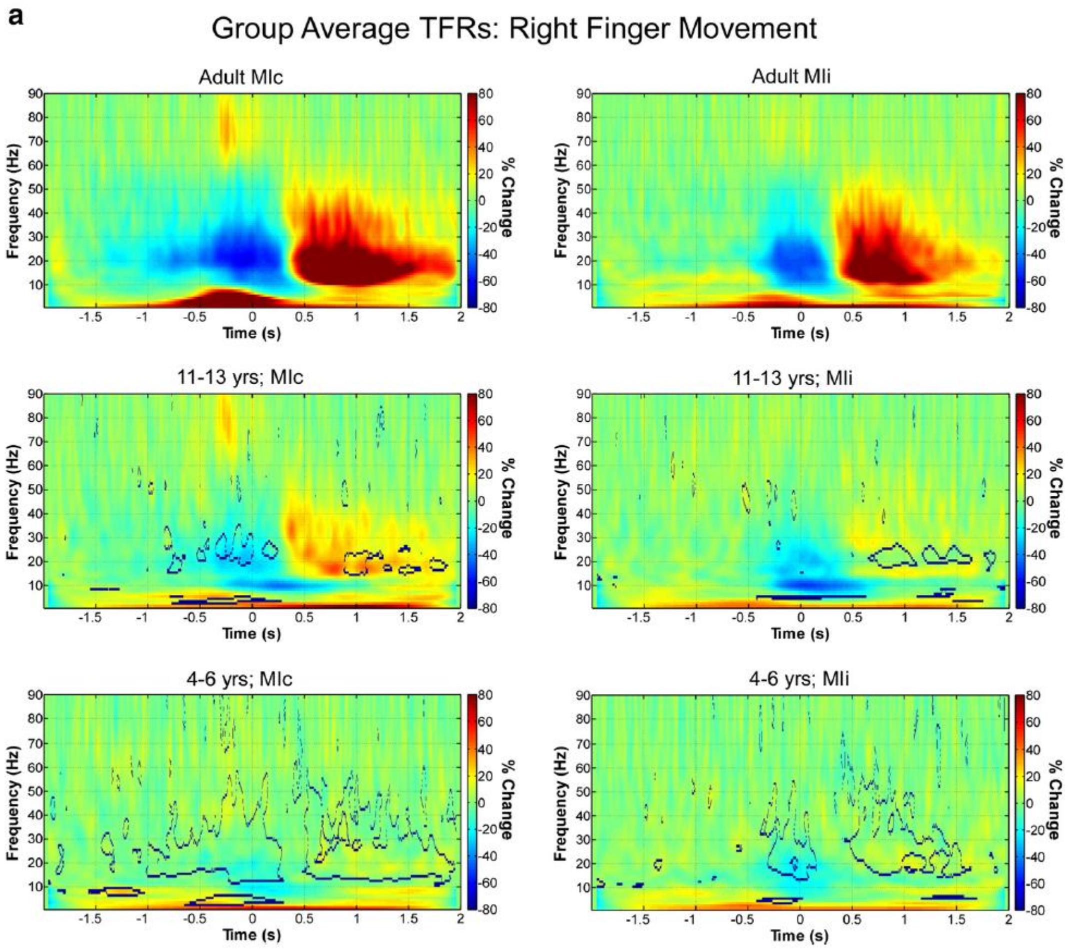
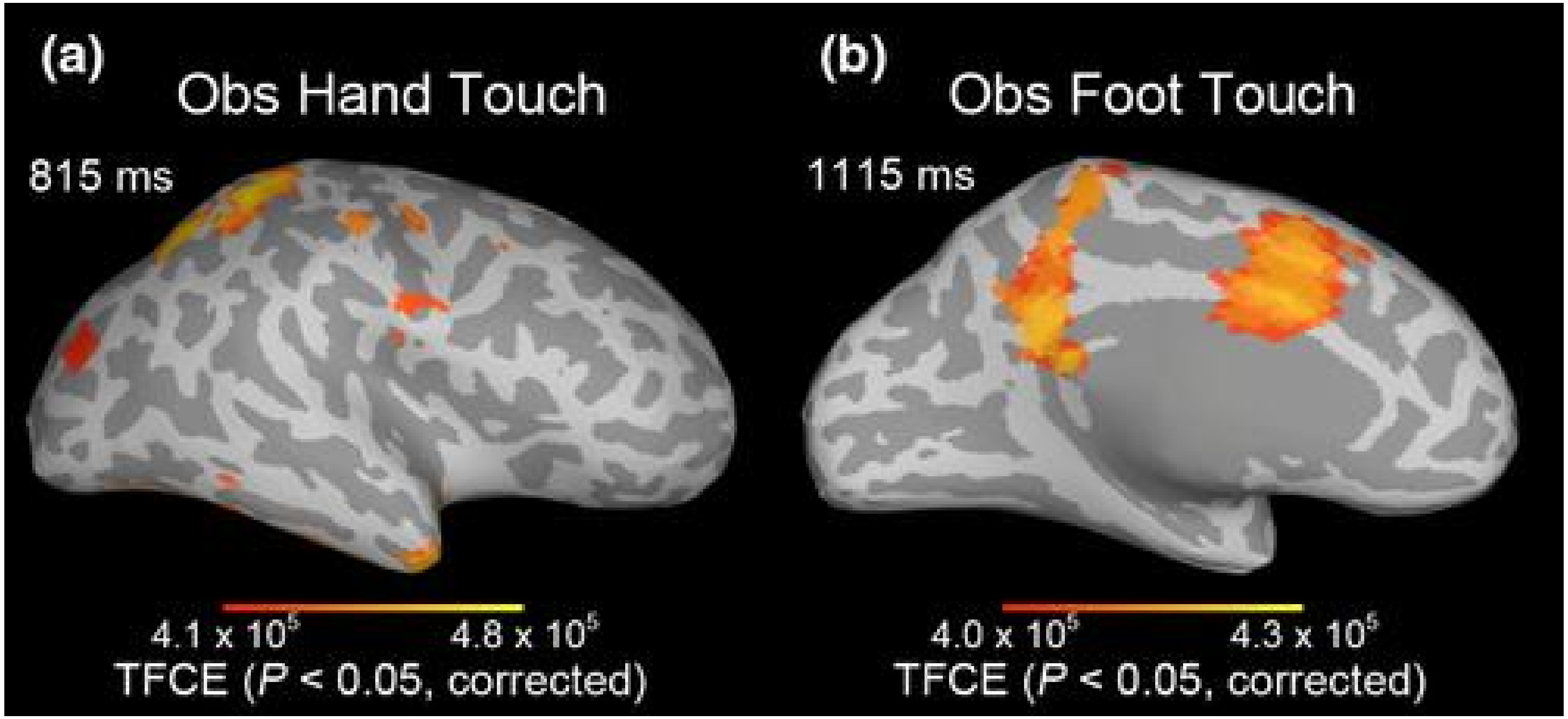


Figure from Gaetz et al., 2010

Beta modulation in 7 mo old infants observing touch



Meltzhoff et al., 2018

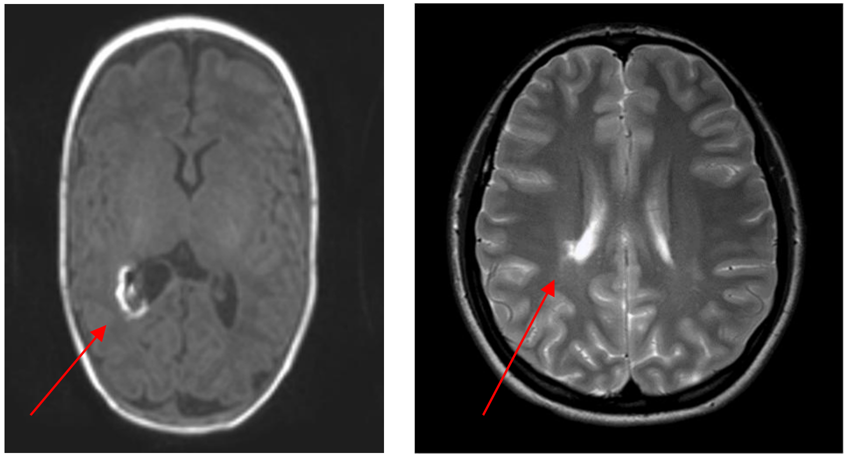
Major types of early focal brain lesions

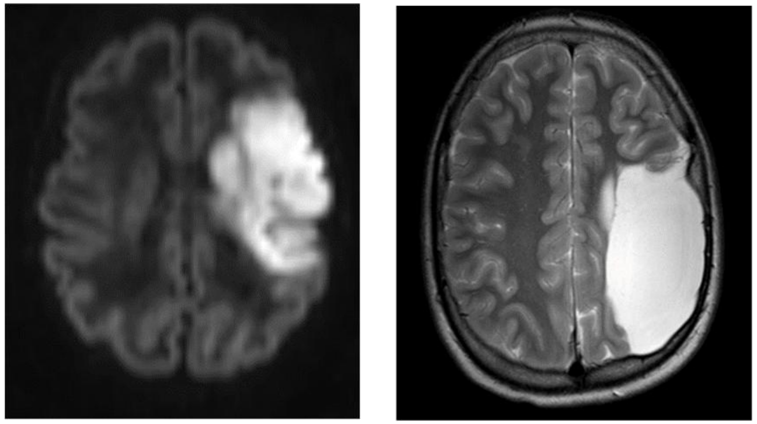
Focal *white* matter injury

- Intraventricular hemorrhage + periventricular *venous* infarction
- Occur during prematurity (< 34 GW)

Focal *gray* matter injury

- *Arterial* ischemic stroke (AIS)
- Typically occur around term age

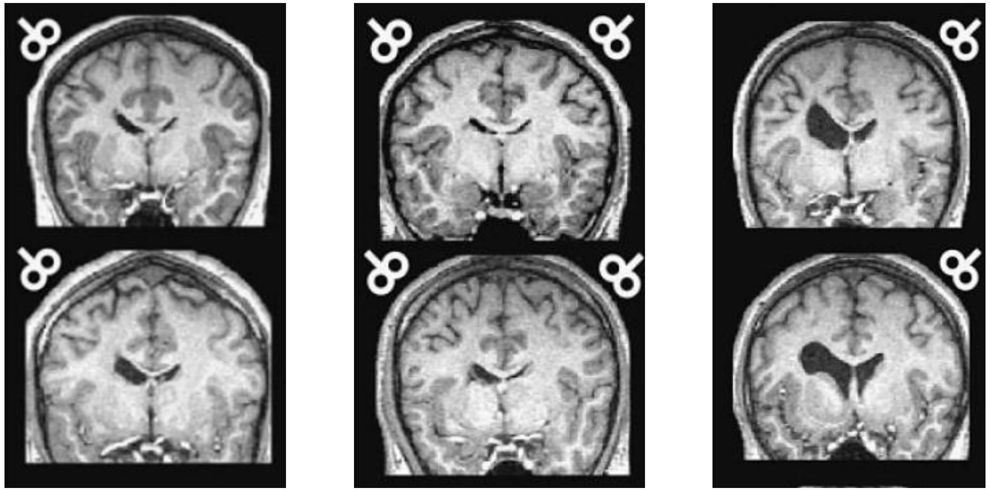


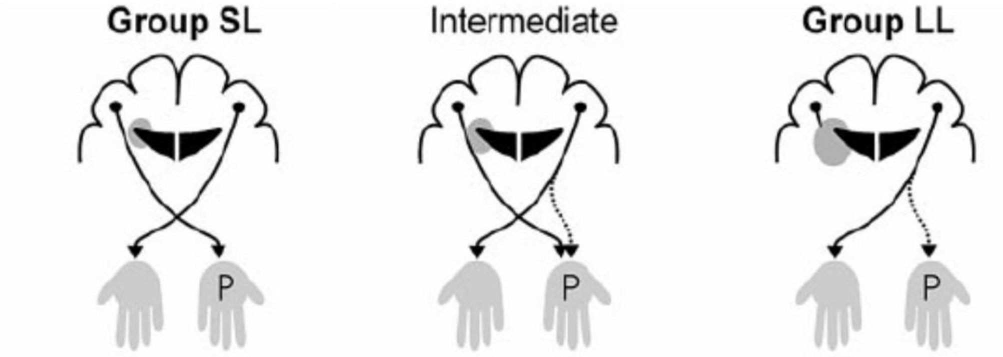


Motor representation in hemiplegic CP (TMS)

Periventricular white matter lesion

Contralateral Bilateral Ipsilateral

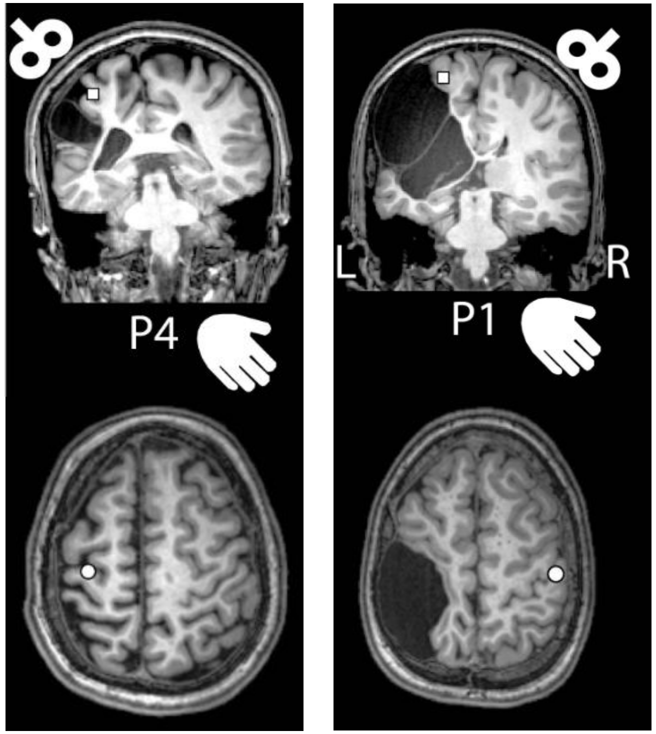




Staudt et al., 2002, Brain

Cortical /corticosubcortical lesion

Contralateral Ipsilateral

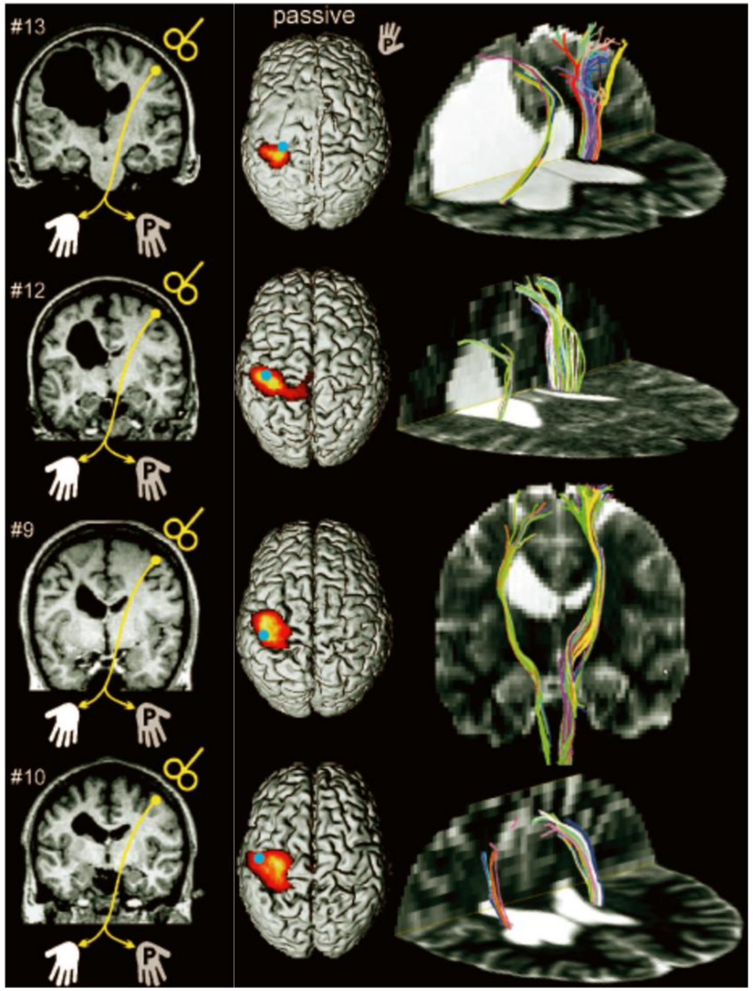


Pihko et al., 2014, HBM

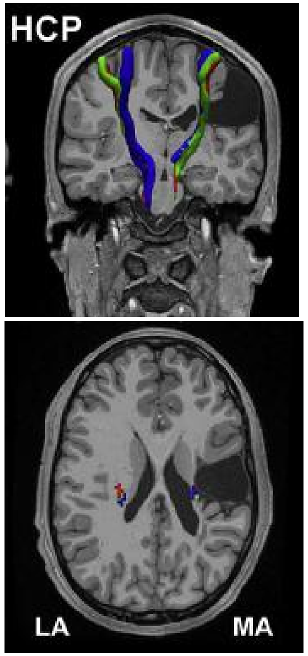
Somatosensory representation in hemiplegic CP (MEG)

Subcortical lesion

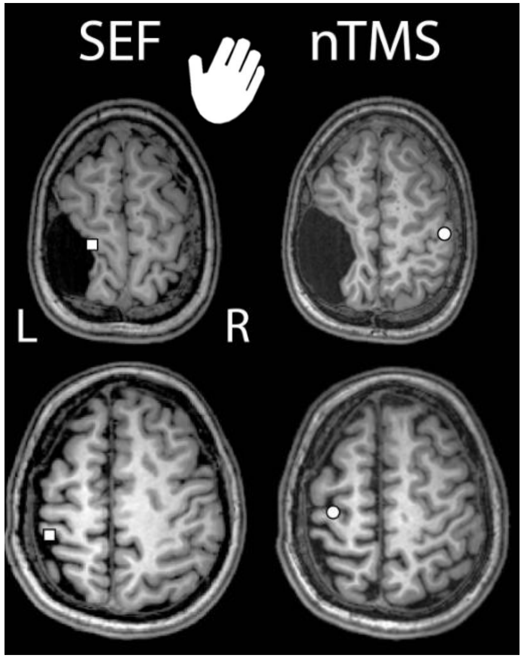
Cortical /corticosubcortical lesion



Staudt et al., 2006



Papadelis et al., 2018



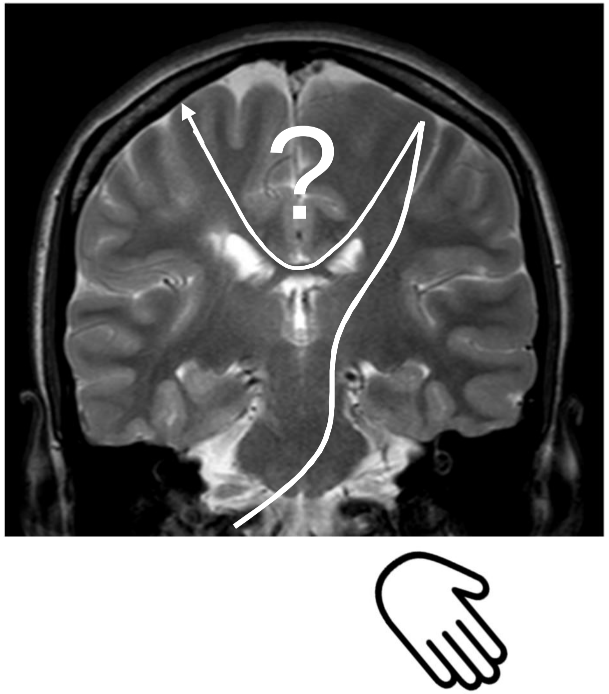
Pihko et al., 2014

Somatosensory representation in hemiplegic CP (MEG)

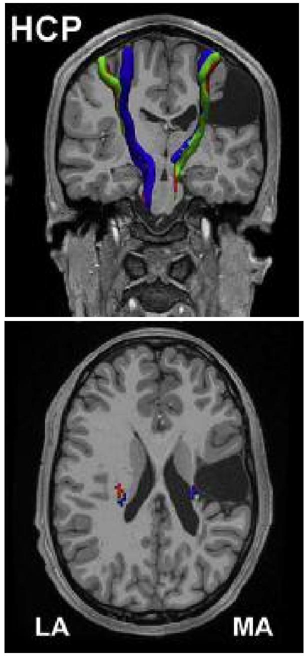
Subcortical lesion

Cortical /corticosubcortical lesion

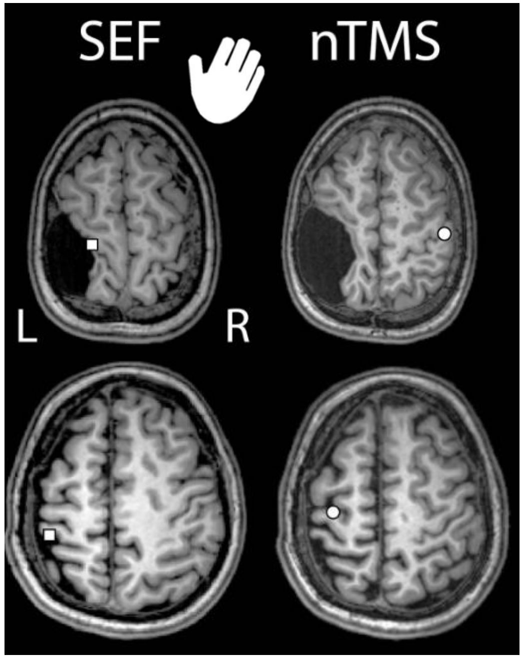
Delayed ipsilateral responses
common in the lesioned hemisphere



Nevalainen et al., 2012

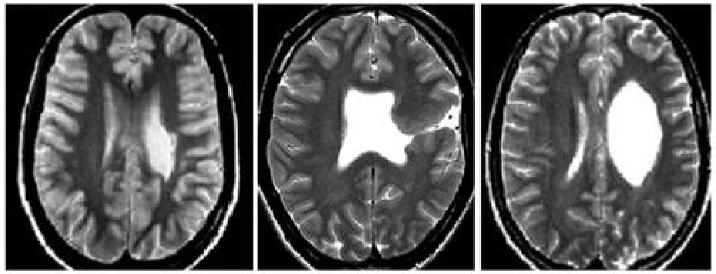


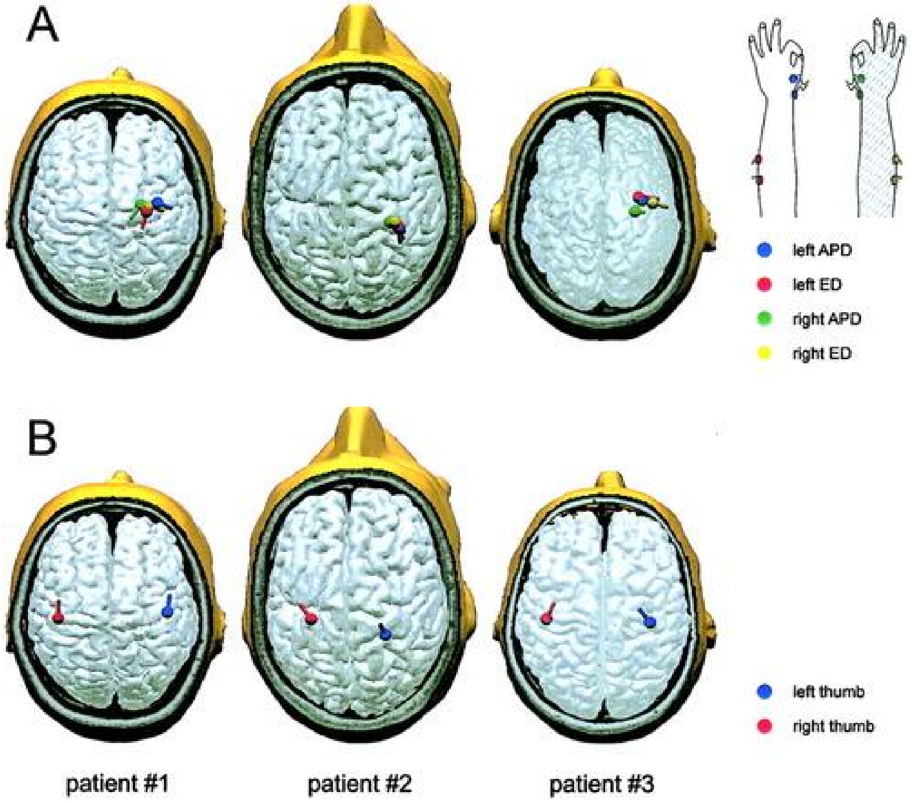
Papadelis et al., 2018



Pihko et al., 2014

Corticomuscular coherence in patients with ipsilateral motor representation (MEG)





CMC contralesional

SEFs ipsilesional

Gerloff et al., 2006, *HBM*

Mechanisms of sensorimotor system plastic adaptation

- Refinement of corticospinal connections activity-dependent
  - tonic levels of spontaneous M1 activity
  - phasic M1 activity reflecting motor control signaling
  - sensory input reflecting limb movement

- Ipsilateral tracts strengthen and contralateral weaken
  - When activity of CS tract is blocked unilaterally (infusion of a GABAa agonist)
  - With unilateral CS tract stimulation (enhancing activity on one side)
  - When movement of one limb (-> and consequently sensory feedback from movement) is blocked by Botox

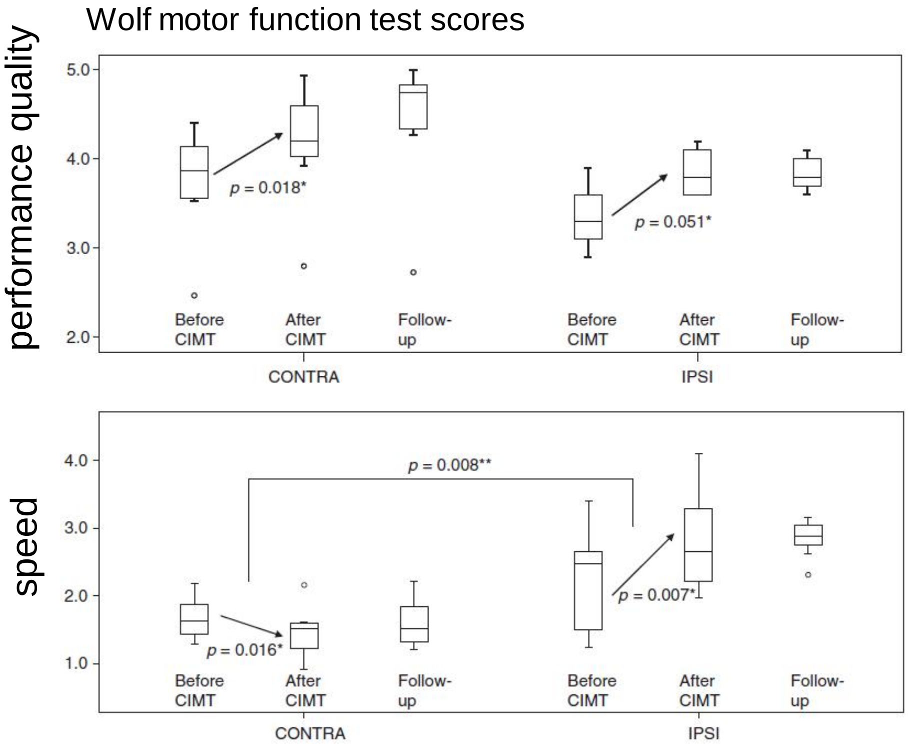
- These changes and the functional deficit are permanent unless treated early by
  - Reducing activity on the nonlesional/non-paretic side
  - Enhancing activity on lesional/paretic side
- At the chronic stage rehabilitation should target activating the remaining tracts

e.g. Martin et al., 2007; Friel et al., 2012; 2014; Carmel et al., 2014

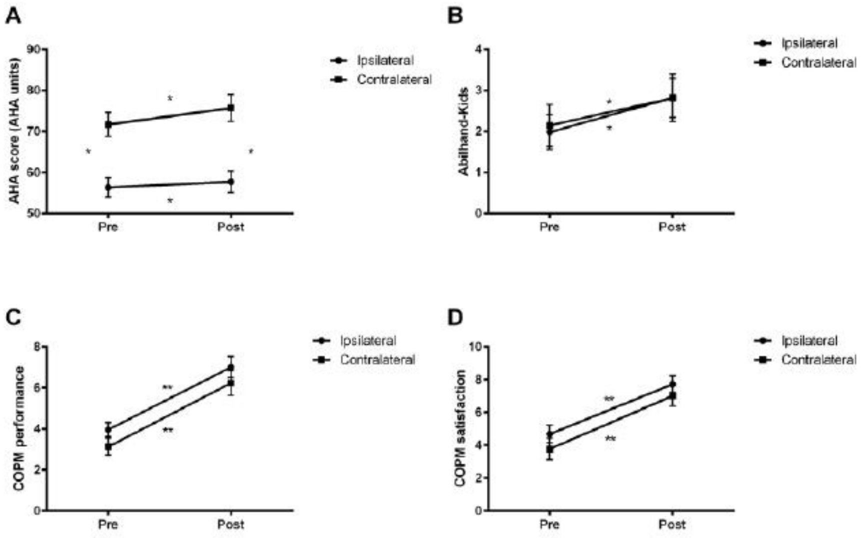
Implications for therapy?

- Constraint-induced movement therapy (CIMT) works better for patients with contralateral hand representation

- Intensive bimanual therapy improves outcomes independent of motor connectivity pattern



Kuhnke et al., 2008 DMCN



Smorenburg et al., 2017

Conclusions

- MEG has significantly contributed to our understanding of early brain development and disease/deficit mechanisms

  -> improvements to clinical practice in the NICU

Conclusions and future

- MEG has provided invaluable information on adaptive plasticity after early brain lesions
  - Future MEG-studies should investigate
    - Beyond the primary hand area
    - Sensorimotor interactions
    - Interhemispheric interactions
    - Longitudinal studies
- Understanding early adaptive plasticity will provide means for individualized therapy
  - MEG one of the methods to define the ”brain wiring” type?
- Early interventions probably more effective
  - MEG to verify therapy induced plastic changes?
- Patient heterogenitity -> large (multicenter?) studies needed

Main collaborators

MEG group
Leena Lauronen, MD PhD
Elina Pihko, PhD

TMS
Selja Vaalto, MD PhD

Clinical neurophysiology
Sampsa Vanhatalo, Prof

Child neurology
Aulikki Lano, MD PhD
Piia Lönnberg, MD
Helena Mäenpää, MD PhD

Neuroimaging
Leena Valanne, MD PhD
Taina Autti, Prof
Sanna Toiviainen-Salo, MD PhD

Neonatology
Marjo Metsäranta, MD PhD
Sture Andersson, Prof
Petri Rahkonen, MD PhD

Thank you!